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TI Gene complementation in the T lymphocyte proliferative response to poly
(Glu57Lys38Tyr5): evidence for effects of polymer handling and gene
dosage

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AB The difficulties encountered in demonstrating Ir gene complementation in
the immune response to the synthetic terpolymer ,
poly(Glu57Lys38Tyr5) (GLT5) were investigated. The method by which the
polymer was put into soln. influenced the outcome because some
determinants on GLT5 were sensitive to exposure to alk. conditions. The
dose of antigen used for immunization was crit. since mice of the H2q
haplotype failed to respond to low doses of GLT5. Prolonged storage of
dialyzed and lyophilized GLT5 led to alterations in the soly. properties
of the polymer with consequent loss of some of the antigenic determinants.
Differences in the genetic make up of the responding strains affected the
overall response. Each responder haplotype recognized different
determinants on the polymer, or the same determinant in different ways,

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Exhibit 38

such that variations in polymer handling appeared to influence selectively the immunogenicity and antigenicity of GLT5 for each strain. Furthermore, the crit. (B10 .times. B10.A)F1 strain, whose response was required to demonstrate conclusively complementation, failed to respond well to certain altered prepns. of the polymer in which the determinants being recognized were present in low concn. This failure, in contrast to the high responsiveness of the genetically similar B10.A(5R) strain, was shown by the low response of [B10.A(4R) .times. B10.A(5R)] F1 mice to result from a gene dosage effect. However, under optimal conditions of antigen handling, (B10 .times. B10.A) F1 mice did respond well to GLT5, demonstrating that 2 complementing Ir genes are involved in the recognition of certain determinants on this polymer.